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Cardiovascular drug medication compliance assessed by dried blood spot sampling techniques

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Abstract

Introduction: Cardiovascular disease is the biggest killer in the UK and yet some 60% of patients are reported not to take their medication correctly. The use of blood spot collection cards was investigated as a means of obtaining small volume samples for the analysis of therapeutic drugs for assessing medication adherence in cardiovascular therapy. An accurate mass liquid chromatography-high resolution mass spectrometry (LC-HRMS) method was developed and validated for the determination of the top three prescribed cardiovascular drugs in the UK, bisoprolol, ramipril and simvastatin, in dried blood spots (DBS).

Methods: For the preparation of DBS samples whole blood spiked with the three target analytes was used to produce 30µl blood spots on specimen collection cards. An 8mm disc was cut from the dried blood spot and extracted using methanol: water (70:30, v/v) containing the internal standard, atenolol. Extracts were vortexed, sonicated and then centrifuged. Analysis was performed using gradient chromatographic elution and a mobile phase flow rate of 0.6ml/min and the column oven temperature at 40°C with a run time of 3 min. MS detection was carried out in electrospray positive ion mode at accurate mass m/z 326.2326 for bisoprolol, m/z 417.2384 for ramipril, m/z 441.2611 for simvastatin and m/z 276.1703 for the IS. The developed bioanalytical method was applied to blood spots samples taken from adult volunteers previously administered one or more of the target drugs.

Results: Drug recoveries from spiked blood spots were ≥92% for bisoprolol and ramipril and ~43% for simvastatin and the drugs were stable in DBS for at least 12 weeks. Validation of the LC-HRMS method showed good linearity and the accuracy and precision values were within the pre-defined limits of ≤15% at all concentrations. Factors with potential to affect drug quantification measurements such as the matrix effects and volume of blood applied onto the collection card were investigated.

	Bisoprolol	Ramipril	Simvastatin
LOQ (S/N >10)	0.5 ng/ml	1.0 ng/ml	5.0 ng/ml

Conclusion: The accurate mass LC-HRMS DBS based method successfully identified control volunteers who were known to be either adherent or non-adherent. There were no false positives from volunteers taking other cardiovascular drugs or from volunteers receiving no medication. Initial research has already identified one case of medication taken incorrectly. This demonstrates that the DBS based assay has the potential to assess patient adherence for a range of therapeutic drugs.

Biography

Sangeeta Tanna is a Reader in Pharmaceutical Bioanalysis in the Leicester School of Pharmacy at De Montfort University. Her expertise and research interests lie in the bioanalysis and drug delivery fields. This has led to the development of micro-analytical methodologies for the determination of therapeutic drugs from dried blood spots (DBS) based on LC-MS and LC-MS/MS studies for a range of clinical applications. This research was awarded the Royal Society of Chemistry Analytical Methods Prize in 2010. Applications of this work to patient care include improved medication for babies and to people with cardiovascular diseases.